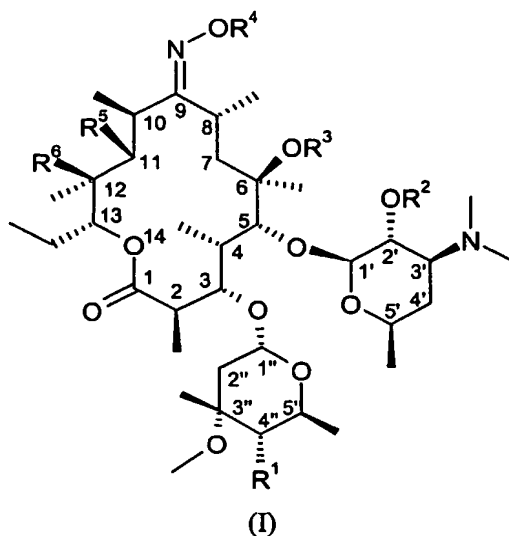


Claims

1. A compound of general formula (I)



wherein

$R^1$  is  $OC(O)(CH_2)_mXR^7$ ;

$R^2$  is hydrogen or a hydroxyl protecting group;

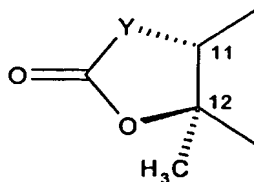
10  $R^3$  is hydrogen,  $C_{1-4}$ alkyl or  $C_{3-6}$ alkenyl optionally substituted by 9 to 10 membered fused bicyclic heteroaryl;

$R^4$  is hydrogen,  $C_{1-4}$ alkyl,  $C_{3-7}$ cycloalkyl,  $C_{3-6}$ alkenyl or a 5 or 6 membered heterocyclic group, wherein the alkyl, cycloalkyl, alkenyl and heterocyclic groups are optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heterocyclic group, optionally substituted 5 or 6 membered heteroaryl,  $OR^8$ ,  $S(O)_nR^8$ ,  $NR^8R^9$ ,  $CONR^8R^9$ , halogen and cyano;

15  $R^5$  is hydroxy,  $C_{3-6}$ alkenyloxy optionally substituted by 9 to 10 membered fused bicyclic heteroaryl, or  $O(CH_2)_pO(CH_2)_qR^{10}$ ,

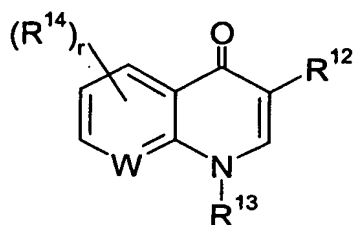
$R^6$  is hydroxy, or

20  $R^5$  and  $R^6$  taken together with the intervening atoms form a cyclic group having the following structure:

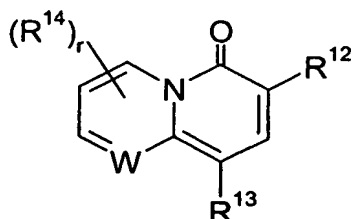


wherein Y is a bivalent radical selected from  $-CH_2-$ ,  $-CH(CN)-$ ,  $-O-$ ,  $-N(R^{11})-$  and  $-CH(SR^{11})-$ ;

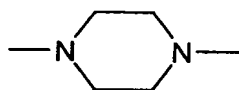
25  $R^7$  is a heterocyclic group having the following structure:



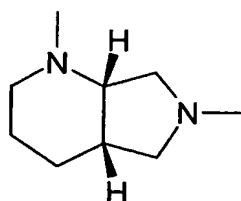
or



- $R^8$  and  $R^9$  are each independently selected from hydrogen and  $C_{1-4}$ alkyl;  
 5  $R^{10}$  is hydrogen or  $NR^8R^9$ ;  
 $R^{11}$  is hydrogen or  $C_{1-4}$ alkyl substituted by a group selected from optionally substituted phenyl, optionally substituted 5 or 6 membered heteroaryl and optionally substituted 9 to 10 membered fused bicyclic heteroaryl;  
 $R^{12}$  is hydrogen,  $C(O)OR^{15}$ ,  $C(O)NHR^{15}$  or  $C(O)CH_2NO_2$ ;  
 10  $R^{13}$  is hydrogen,  $C_{1-4}$ alkyl optionally substituted by hydroxy or  $C_{1-4}$ alkoxy,  $C_{3-7}$ cycloalkyl, or optionally substituted phenyl or benzyl;  
 $R^{14}$  is halogen,  $C_{1-4}$ alkyl,  $C_{1-4}$ thioalkyl,  $C_{1-4}$ alkoxy,  $NH_2$ ,  $NH(C_{1-4}alkyl)$  or  $N(C_{1-4}alkyl)_2$ ;  
 $R^{15}$  is hydrogen or  $C_{1-4}$ alkyl optionally substituted by up to three groups independently  
 15 selected from halogen,  $C_{1-4}$ alkoxy,  $OC(O)C_{1-4}alkyl$  and  $OC(O)OC_{1-4}alkyl$ ;  
 $R^{16}$  is hydrogen,  $C_{1-4}$ alkyl,  $C_{3-7}$ cycloalkyl, optionally substituted phenyl or benzyl, acetyl or benzoyl;  
 $R^{17}$  is hydrogen or  $R^{14}$ , or  $R^{17}$  and  $R^{13}$  are linked to form the bivalent radical  $-O(CH_2)_2-$  or  $-(CH_2)_v-$ ;  
 20  $X$  is  $-U(CH_2)_5Z-$  or  $X$  is a group selected from:



and



- 25  $U$  and  $Z$  independently are a divalent radical selected from  $-N(R^{16})-$ ,  $-O-$ ,  $-S(O)_t-$ ,  $-N(R^{16})C(O)-$ ,  $-C(O)N(R^{16})-$  and  $-N[C(O)R^{16}]-$ ;  
 $W$  is  $CR^{17}$  or a nitrogen atom;  
 $m$  is 0 or an integer from 1 to 5;

n, r and t are each independently selected from 0, 1 and 2;  
 p and q are each independently selected from 1 to 6 ;  
 s is an integer from 2 to 8; and  
 v is 2 or 3;

5 and pharmaceutically acceptable derivatives thereof.

2. A compound according to claim 1 wherein  $R^2$  is hydrogen.

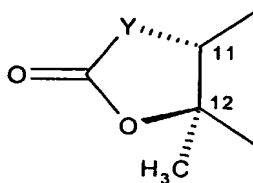
3. A compound according to claim 1 or 2 wherein  $R^3$  is hydrogen.

10

4. A compound according to any one of the preceding claims wherein  $R^4$  is hydrogen or  $C_{1-4}$ alkyl optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heteroaryl,  $OR^8$ ,  $S(O)_nR^8$ ,  $NR^8R^9$ , halogen and cyano.

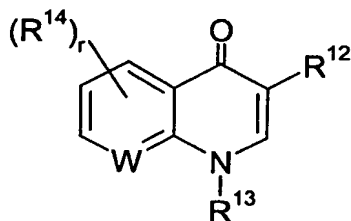
15

5. A compound according to any one of the preceding claims wherein  $R^5$  is hydroxy or  $O(CH_2)_pO(CH_2)_qR^{10}$  and  $R^6$  is hydroxy, or  $R^5$  and  $R^6$  taken together with the intervening atoms form a cyclic group having the following structure:



20 wherein Y is the bivalent radical -O-.

6. A compound according to any one of the preceding claims wherein  $R^7$  is a heterocyclic group having the following structure:



25

wherein W is  $CR^{17}$  where  $R^{17}$  is hydrogen.

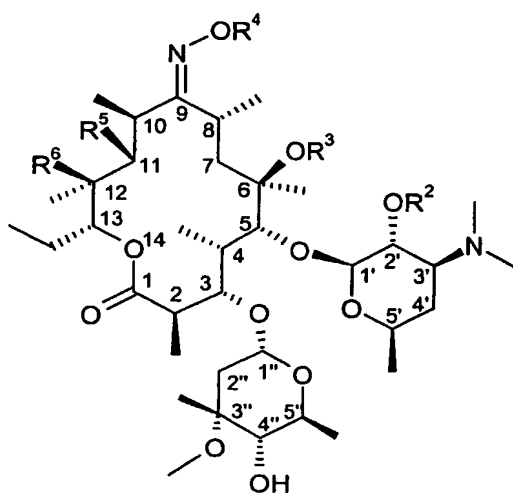
7. A compound according to any one of the preceding claims wherein X is  $-U(CH_2)_sZ-$  wherein U and Z are independently -NH- or -O-.

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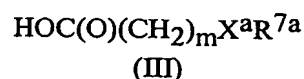
8. A compound according to claim 1 as defined in any one of Examples 1 to 15, or a pharmaceutically derivative thereof.

9. A compound selected from:

- 4''-O-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinoliny) amino]ethyl]amino]propionyl]-11-O-(2-dimethylaminoethoxymethyl)-(9E)-methoximino erythromycin A,
- 5 4''-O-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinoliny) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-O-(2-propyl)oximino erythromycin A,
- 4''-O-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinoliny) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-methoximino erythromycin A, and
- 10 4''-O-[3-[[2-[(3-carboxy-7-chloro-1-cyclopropyl-1,4-dihydro-4-oxo-6-quinoliny) amino]ethyl]amino]propionyl]-11,12-carbonate-(9E)-O-(ethoxymethyl)oximino erythromycin A,
- or a pharmaceutically acceptable derivative thereof.
- 15 10. A process for the preparation of a compound as claimed in claim 1 which comprises:
- a) reacting a compound of formula (II)



(II)

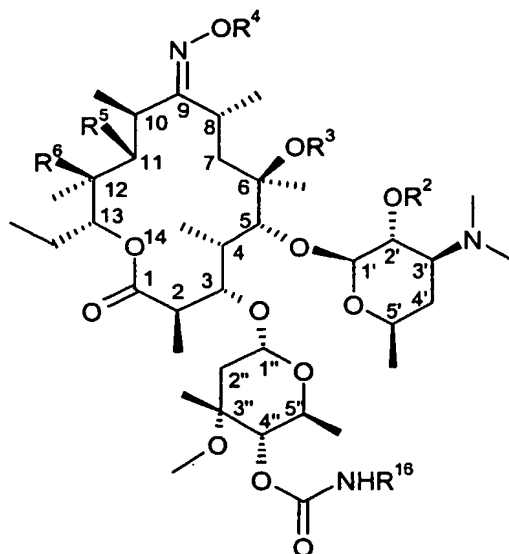


with a suitable activated derivative of the acid (III), wherein m is an integer 1 to 5,  $\text{X}^a$  and  $\text{R}^{7a}$  are X and  $\text{R}^7$  as defined in claim 1 or groups convertible to X and  $\text{R}^7$ , to produce a compound of formula (I) wherein m is an integer 1 to 5;

25

- b) reacting a compound of formula (II), in which the 4'' hydroxy is suitably activated, with a compound of formula  $\text{X}^a\text{R}^{7a}$  (IV), wherein  $\text{R}^{7a}$  is  $\text{R}^7$  as defined in claim 1 or a group convertible to  $\text{R}^7$ , s and Z have the meanings defined in claim 1 and  $\text{X}^a$  is  $-\text{U}(\text{CH}_2)_s\text{Z}-$  or a group convertible to  $-\text{U}(\text{CH}_2)_s\text{Z}-$ , in which U is a group selected from selected from -N( $\text{R}^{16}$ )-, -O-, and -S-, to produce a compound of formula (I) wherein m is 0 and U is a group selected from -N( $\text{R}^{16}$ )-, -O- and -S-;
- 30

- c) reacting a compound of formula (V)

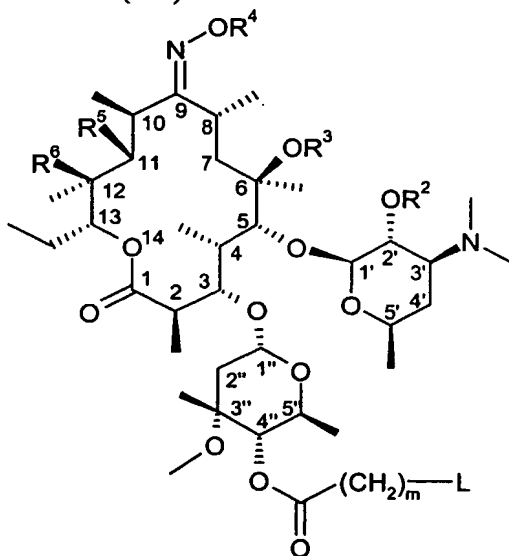


(V)

wherein R<sup>16</sup> has the meaning defined in claim 1 with a suitable activated derivative of the carboxylic acid HOC(O)(CH<sub>2</sub>)<sub>s</sub>Z<sup>a</sup>R<sup>7a</sup> (VI), wherein R<sup>7a</sup> and Z<sup>a</sup> are R<sup>7</sup> and Z as defined in claim 1 or groups convertible to R<sup>7</sup> and Z, to produce a compound of formula (I) wherein m is 0 and U is -N(R<sup>16</sup>)C(O)-;

d) reacting a compound of formula (II) with a suitably activated derivative of the carboxylic acid HOC(O)C(O)N(R<sup>16</sup>)(CH<sub>2</sub>)<sub>s</sub>Z<sup>a</sup>R<sup>7a</sup> (VIIb) to produce a compound of formula (I) wherein m is 0 and U is -C(O)N(R<sup>16</sup>)-;

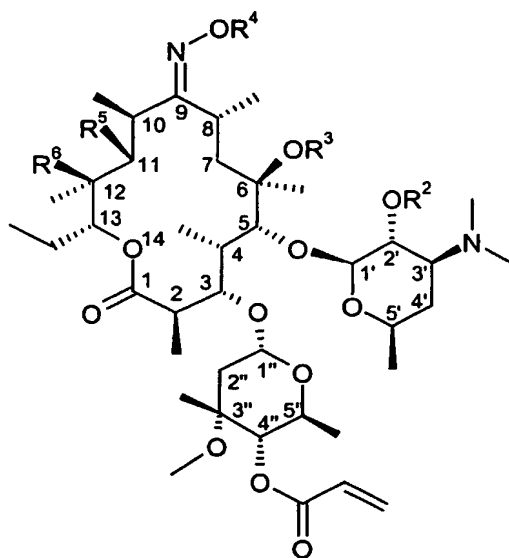
e) reacting a compound of formula (VII)



(VII)

with a compound of formula X<sup>a</sup>R<sup>7a</sup> (IV), wherein R<sup>7a</sup> and X<sup>a</sup> are R<sup>7</sup> and X as defined in claim 1 or groups convertible to R<sup>7</sup> and X, U is a group selected from -N(R<sup>16</sup>)-, -O- and -S-, and L is suitable leaving group, to produce a compound of formula (I) wherein m is 1 to 5 and U is a group selected from -N(R<sup>16</sup>)-, -O- and -S-; or

f) reacting a compound of formula (IX), with a compound of formula  $X^aR^{7a}$  (IV),



(IX)

wherein  $R^{7a}$  and  $X^a$  are  $R^7$  and  $X$  as defined in claim 1 or groups convertible to  $R^7$  and  $X$ ,  $U$  is a group selected from  $-N(R^{16})-$ ,  $-O-$  and  $-S-$ , to produce a compound of formula (I) wherein  $m$  is 2 and  $U$  is a group selected from  $-N(R^{16})-$ ,  $-O-$  and  $-S-$ ;

and thereafter, if required, subjecting the resulting compound to one or more of the following operations:

- i) removal of the protecting group  $R^2$ ,
- ii) conversion of  $X^aR^{7a}$  or  $Z^aR^{7a}$  to  $XR^7$  or  $ZR^7$  respectively, and
- iii) conversion of the resultant compound of formula (I) into a pharmaceutically acceptable derivative thereof.

11. A compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in therapy.

12. The use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in the preparation of a medicament for use in the therapy of systemic or topical microbial infections in a human or animal body.

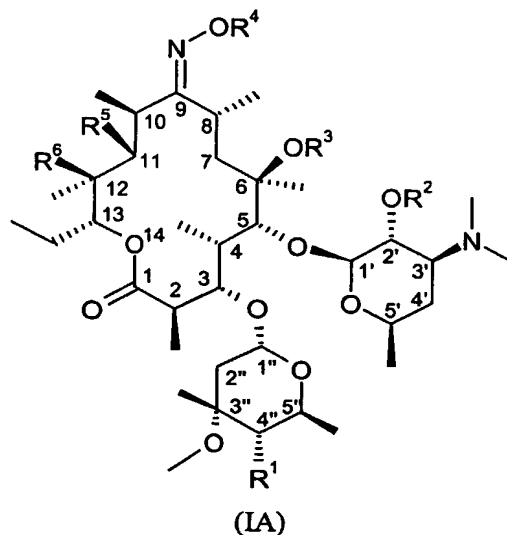
13. The use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in the treatment or prophylaxis of systemic or topical microbial infections in a human or animal body.

14. A pharmaceutical composition comprising a compound as claimed any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in admixture with one or more pharmaceutically acceptable carriers or excipients.

15. A method for the treatment of the human or non-human animal body to combat microbial infection comprising administration of an effective amount of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof.

5

16. A compound of general formula (IA)



10 wherein

$R^1$  is  $OC(O)(CH_2)_mXR^7$ ;

$R^2$  is hydrogen or a hydroxyl protecting group;

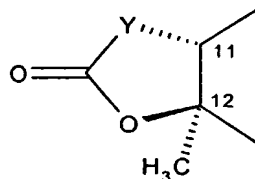
$R^3$  is hydrogen,  $C_{1-4}$ alkyl or  $C_{3-6}$ alkenyl optionally substituted by 9 to 10 membered fused bicyclic heteroaryl;

15  $R^4$  is hydrogen,  $C_{1-4}$ alkyl,  $C_{3-7}$ cycloalkyl,  $C_{3-6}$ alkenyl or a 5 or 6 membered heterocyclic group, wherein the alkyl, cycloalkyl, alkenyl and heterocyclic groups are optionally substituted by up to three substituents independently selected from optionally substituted 5 or 6 membered heterocyclic group, optionally substituted 5 or 6 membered heteroaryl,  $OR^8$ ,  $S(O)_nR^8$ ,  $NR^8R^9$ ,  $CONR^8R^9$ , halogen and cyano;

20  $R^5$  is hydroxy,  $C_{3-6}$ alkenyloxy optionally substituted by 9 to 10 membered fused bicyclic heteroaryl or  $O(CH_2)_pO(CH_2)_qR^{10}$ ,

$R^6$  is hydroxy, or

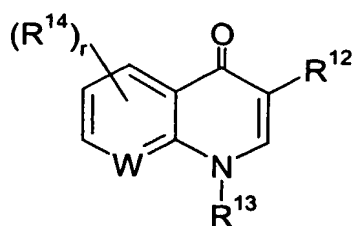
$R^5$  and  $R^6$  taken together with the intervening atoms form a cyclic group having the following structure:



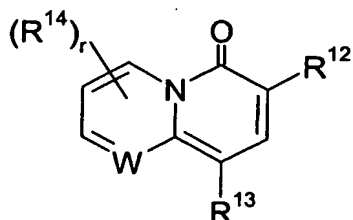
25

wherein Y is a bivalent radical selected from  $-CH_2-$ ,  $-CH(CN)-$ ,  $-O-$ ,  $-N(R^{11})-$  and  $-CH(SR^8)-$ ;

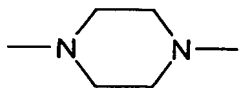
$R^7$  is a heterocyclic group having the following structure:



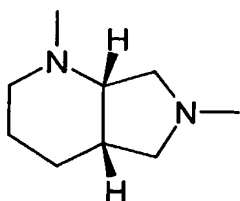
or



- 5 R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen and C<sub>1-4</sub>alkyl;  
 R<sup>10</sup> is hydrogen or NR<sup>8</sup>R<sup>9</sup>;  
 R<sup>11</sup> is hydrogen or C<sub>1-4</sub>alkyl substituted by a group selected from optionally substituted phenyl, optionally substituted 5 or 6 membered heteroaryl and optionally substituted 9 to 10 membered fused bicyclic heteroaryl;  
 10 R<sup>12</sup> is hydrogen, C(O)OR<sup>15</sup>, C(O)NHR<sup>15</sup> or C(O)CH<sub>2</sub>NO<sub>2</sub>;  
 R<sup>13</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, or optionally substituted phenyl or benzyl;  
 R<sup>14</sup> is halogen, C<sub>1-4</sub>alkyl, C<sub>1-4</sub>thioalkyl, C<sub>1-4</sub>alkoxy, NH<sub>2</sub>, NH(C<sub>1-4</sub>alkyl) or N(C<sub>1-4</sub>alkyl)<sub>2</sub>;  
 R<sup>15</sup> is hydrogen or C<sub>1-4</sub>alkyl;  
 15 R<sup>16</sup> is hydrogen, C<sub>1-4</sub>alkyl, C<sub>3-7</sub>cycloalkyl, optionally substituted phenyl or benzyl, acetyl or benzoyl;  
 X is -U(CH<sub>2</sub>)<sub>s</sub>Z- or X is a group selected from:



and



20

- U and Z independently are a divalent radical selected from -N(R<sup>16</sup>)-, -O-, -S(O)<sub>t</sub>-,  
 N(R<sup>16</sup>)C(O)-, -C(O)N(R<sup>16</sup>)- and -N[C(O)R<sup>16</sup>]-;  
 W is a carbon or a nitrogen atom;  
 25 m is 0 or an integer from 1 to 5;  
 n, r and t are each independently selected from 0, 1 and 2;  
 p and q are each independently selected from 1 and 2; and  
 s is an integer from 2 to 8;

and pharmaceutically acceptable salts and solvates thereof.